

**Amendments to the Specification:**

Please replace the table bridging pages 12 and 13, with the following amended table:

SEQUENCE	AUTHOR/YEAR	NO
Vitamin D binding	Perlmann <i>et al</i> 1993	1
Serum response	Pollock <i>et al</i> 1991	2
CREB/ATF	Liu and Green 1990	3
Myb (reverse)	Faisst and Meyer 1992	4
AP4	Hu <i>et al</i> 1990	5
AP1	Yen <i>et al</i> 1991	6
CTF-NF1	Gronostajski 1987	7
(CTF-NF1) Octamer	Ruvkun and Finney 1991	8
AP2	Williams and Tijina 1991	9
ISRE reverse	Tanaka <i>et al</i> 1993	10
CTF-NF1	Gronostajski 1987	11
CPB	Graves <i>et al</i> 1986	12
SP1	Kadonaga <i>et al</i> 1987	13
CREB/ATF	Liu and Green 1990	14
C-Jun	Mitchell and Tjian 1989	15
CBP	Graves <i>et al</i> 1986	16
NFκB	Virbasius 1993	17
AP1	Yen <i>et al</i> 1991	18
NFκB	Virbasius, 1993	19
c-Jun	Mitchell and Tjian 1989	20

SP1	Kadonaga <i>et al</i> 1987	21
$\alpha$ -IFN	Fujita <i>et al</i> 1985	22
AP1	Yen <i>et al</i> 1991	23
$\alpha$ -IFN	Fujita <i>et al</i> 1985	24
NF $\kappa$ B	Virbasius, 1993	25
SP1	Kadonaga <i>et al</i> 1987	26
CBP	Graves <i>et al</i> 1986	27
SP1	Kadonaga <i>et al</i> 1987	28
TFIIB	Breathnack and Chambon 1981	29
TFIID	Breathnack and Chambon 1981	30
Initiator	Smale and Baltimore, 1989	31
AP2	Williams and Tijian 1991	32
Downstream element	Burke <i>et al</i> 1998	33
GAGCTCTCAGTCTCAGCGA TCAA <u>(SEQ ID NO:34)</u>		34

Please replace the paragraph at page 26, lines 10 through 23, with the following amended paragraph:

The promoter and enhancer parts of the exemplary chemically synthesized promoters disclosed herein were designed according to the currently available knowledge of the transcription mechanisms of RNA polymerase II and partly by trial of different combinations and permutations of the oligonucleotide sequences. Each construct was centered by a TATA box (Burke *et al.*, 1998) (here TATATAA (SEQ ID NO:30); TFIID, Breathnach and Chambon 1981) with the initiator at position +1 (here TCATTC (SEQ ID NO:39), Initiator, Smale and Baltimore, 1989). Various transcription factors binding sites and other elements were added upstream and downstream of the TATA box in these exemplary examples. These sites and elements are underlined and indicated in parenthesis, after each specific sequence as in Examples 1, 2 and 3 below and Table 1. In the sequences described below lack of underlining represents spacing regions which may vary but usually follows the following rule as discussed elsewhere in the specification: the spacing region may have approximately equal distribution of adenine, guanine, cytosine and thymine bases and may further be comprised of three consecutive adenine or thymine bases.

Please replace the paragraph at page 27, lines 4 through 31, with the following amended paragraph:

CGGTACATGATGTTCTCGATGCAATATCACGTGAAGGTCAAAAATAGGTCA (SEQ ID NO:1) (Vitamin D binding element, Perlmann *et al.*, 1993) AGGTCACCTCTCTCGGCT (SEQ ID NO:2) (serum response element, Pollock *et al.*, 1991) ATCAAATAAGAGTGTAGGGACGGGAGAGGGGGAAAACAGAACAGAGTGTGACGTCA (SEQ ID NO:3) (CREB/ATF element, Liu and Green, 1990) GCAGGCAGTTG (SEQ ID NO:4) (Myb element, reverse, Faisst and Meyer, 1992) CCCTTTGAAAA CGTTAACGTTAACGTTTCACTGCAGCTGCA (SEQ ID NO:5) (AP4 element, Hu *et al.*, 1990) GCTGATTAA (SEQ ID NO:6) (AP1, Yen *et al.*, 1991) TAATTACAGCCAA (SEQ ID NO:7) (CTF-NF1, Gronostajski, 1987) AGGCGCCAAAGGCAACGTTATATGCAAATATGCAAA (SEQ ID NO:8) (Octamer element, Ruvkun and Finney, 1991) TGAGAACAGGGGGGGGGGGCGG (SEQ ID NO:9) (AP2, Williams and Tjian, 1991) ACATCGGTTCAACGTTTCTGGTTTCAATTTCTCTTCT (SEQ ID NO:10) (ISRE reverse, Tanaka *et al.*, 1993) ATTAATAATTACCGTTGGCCATTAGCCA (SEQ ID NO:11) (CTF-NF1, Gronostajski, 1987) TATCCAAT (SEQ ID NO:12) (CBP element, Graves *et al.*, 1986) GGGGCGGG (SEQ ID NO:13) (SP1, Kadonaga *et al.*, 1987) ATTTGACGTCA (SEQ ID NO:14) (CREB/ATF, Liu and Green 1990) ATAATGAC (SEQ ID NO:15) (C-Jun, Mitchell and Tjian, 1989) GCCAAT (SEQ ID NO:16) (CBP element, Graves *et al.*, 1986) AGGGACTTTCC (SEQ ID NO:17) (NFkB, Virbasius, 1993) GACTCAC (SEQ ID NO:18) (AP1, Yen *et al.*, 1991) GGGGATTTC (SEQ ID NO:19) (NFkB element, Virbasius *et al.*, 1993) CAAC GTTTTGGTTGACGAA (SEQ ID NO:20) (C-Jun element, Mitchell and Tjian, 1989) ATGGGCGG (SEQ ID NO:21) (SP1 element, Kadonaga, *et al.*, 1987) TGTAAATGACATA (SEQ ID NO:22) ( $\alpha$ -IFN, Fujita *et al.*, 1985) GGAAAACTGACTCA (SEQ ID NO:23) (AP1, Yen *et al.*, 1991) CAAAGGGAGAAGTGA (SEQ ID NO:24) ( $\alpha$ -IFN, Fujita *et al.*, 1985) AAGTGGGACTTTCC (SEQ ID NO:25) (NFkB, Virbasius *et al.*, 1993) AAAGGGCGG (SEQ ID NO:26) (SP1, Kadonaga, *et al.*, 1987) CCAAT (SEQ ID NO:27) (CBP, Graves *et al.*, 1986) TGTGGGCGGG (SEQ ID NO:28) (SP1, Kadonaga, *et al.*, 1987) CCACCGGTGTTCTGAAGGGCGCC (SEQ ID NO:29) (TFIIB) TATATAA (SEQ ID NO:30) (TFIID, Breathnach and Chambon, 1981) GGGGGGGCGGGCGCGTTCGTCCTCATTC (SEQ ID NO:31) (Initiator, Smale and Baltimore, 1989) TGGACCGCGTCCGCCCCGCG (SEQ ID NO:32) (AP2, Williams and Tjian, 1991) AGCAGACGTG (SEQ ID NO:33) (downstream element, Burke *et al.*, 1998) GAGCTCTCAGTCTCAGCGATCAA (SEQ ID NO:34).

Please replace the paragraph at page 28, lines 8 through 31, with the following amended paragraph:

## **EXAMPLE 2**

### **SP72 PROMOTER/ENHANCER LESS THE SRE (SERUM RESPONSE ELEMENT)**

The inventors generated a further exemplary promoter/enhancer sequence of SEQ. ID NO:37 using methods as is known to the skilled artisan and described herein, by deleting the SRE of the exemplary promoter/enhancer of SEQ. ID NO:36, thereby obtaining a further promoter/enhancer as detailed below:

CGGTACATGATGTTCTCGATGCAATATCACGTGAAGGTCAAAAATAGGTCA (SEQ ID NO:1) (Vitamin D binding element, Perlmann *et al.*, 1993) ATCAAATAAGAGTGTAGGGACGGGAGAGGGGAAAACAGAACAGACAGTGCTGACGTCA (SEQ ID NO:3) (CREB/ATF element, Liu and Green, 1990) GCAGGCAGTTG (SEQ ID NO:4) (Myb element, reverse, Faisst and Meyer, 1992) CCCTTTGAAAA CGTTAACGTTAACGTTCACTGCTGCACTGCA (SEQ ID NO:5) (AP4 element, Hu *et al.*, 1990) GCTGATTAA (SEQ ID NO:6) (AP1, Yen *et al.*, 1991) TAATTACAGCCAA (SEQ ID NO:7) (CTF-NF1, Gronostajski, 1987) AGGCGCCAAAGGCAACGTTATATGCAAATATGCAAA (SEQ ID NO:8) (Octamer element, Ruvkun and Finney, 1991) TGAGAACAGGGGGGGGGGGCGG (SEQ ID NO:9) (AP2, Williams and Tjian, 1991) ACATCGGTTCAACGTTTCTGGTTTCAATTTCTCTTCT (SEQ ID NO:10) (ISRE reverse, Tanaka *et al.*, 1993) ATTAATAATTACCGTTGGCCATTAGCCA (SEQ ID NO:11) (CTF-NF1, Gronostajski, 1987) TATCCAAT (SEQ ID NO:12) (CBP element, Graves *et al.*, 1986) GGGGCGGG (SEQ ID NO:13) (SP1, Kadonaga *et al.*, 1987) ATTTGACGTCA (SEQ ID NO:14) (CREB/ATF, Liu and Green 1990) ATAATGAC (SEQ ID NO:15) (C-Jun, Mitchell and Tjian, 1989) GCCAAT (SEQ ID NO:16) (CBP element, Graves *et al.*, 1986) AGGGACTTTCC (SEQ ID NO:17) (NFkB, Virbasius, 1993) GACTCAC (SEQ ID NO:18) (AP1, Yen *et al.*, 1991) GGGGATTTC (SEQ ID NO:19) (NFkB element, Virbasius *et al.*, 1993) CAAC GTTTTGGTTGACGAA (SEQ ID NO:20) (C-Jun element, Mitchell and Tjian, 1989) ATGGGCGG (SEQ ID NO:21) (SP1 element, Kadonaga, *et al.*, 1987) TGTAATGACATA (SEQ ID NO:22) ( $\alpha$ -IFN, Fujita *et al.*, 1985) GGAAACTGACTCA (SEQ ID NO:23) (AP1, Yen *et al.*, 1991) CAAAGGGAGAAGTGA (SEQ ID NO:24) ( $\alpha$ -IFN, Fujita *et al.*, 1985) AAGTGGGACTTTCC (SEQ ID NO:25) (NFkB, Virbasius *et al.*, 1993) AAAGGGCGG (SEQ ID NO:26) (SP1, Kadonaga, *et al.*, 1987) CCAAT (SEQ ID NO:27) (CBP, Graves *et al.*, 1986) TGTGGGCGGG (SEQ ID NO:28) (SP1, Kadonaga, *et al.*, 1987)

CCACCGGTGTTCTGAAGGGCGCC (SEQ ID NO:29) (TFIIB) TATATAA (SEQ ID NO:30) (TFIID, Breathnach and Chambon, 1981) GGGGGGGCGGGCGCGTTCGTCCTCATTC (SEQ ID NO:30) (Initiator, Smale and Baltimore, 1989) TGGACCGCGTCCGCCCGCG (SEQ ID NO:32) (AP2, Williams and Tjian, 1991) AGCAGACGTG (SEQ ID NO:33) (downstream element, Burke *et al.*, 1998) GAGCTCTCAGTCTCAGCGATCAA (SEQ ID NO:34).

Please replace the paragraph at page 29, lines 1-16, with the following amended paragraph:

### **EXAMPLE 3**

#### **SP72 PROMOTER SEQUENCE**

In a further embodiment of the invention, the promoter sequence (SEQ. ID NO:35) of SP72 is provided, as detailed below:

AAATGACATA (SEQ ID NO:40) ( $\alpha$ -IFN, Fujita *et al.*, 1985) GGAAAACTGACTCA (SEQ ID NO:23) (AP1, Yen *et al.*, 1991) CAAAGGGAGAAGTGA (SEQ ID NO:24) ( $\alpha$ -IFN, Fujita *et al.*, 1985) AAGTGGGACTTTCC (SEQ ID NO:25) (NF $\kappa$ B, Virbasius *et al.*, 1993) AAAGGGCGG (SEQ ID NO:26) (SP1, Kadonaga, *et al.*, 1987) CCAAT (SEQ ID NO:27) (CBP, Graves *et al.*, 1986) TGTGGGCGGGG (SEQ ID NO:28) (SP1, Kadonaga, *et al.*, 1987) CCACCGGTGTTCTGAAGGGCGCC (SEQ ID NO:29) (TFIIB) TATATAA (SEQ ID NO:30) (TFIID, Breathnach and Chambon, 1981) GGGGGGGCGGGCGCGTTCGTCCTCATTC (SEQ ID NO:31) (Initiator, Smale and Baltimore, 1989) TGGACCGCGTCCGCCCGCG (SEQ ID NO:32) (AP2, Williams and Tjian, 1991) AGCAGACGTG (SEQ ID NO:33) (downstream element, Burke *et al.*, 1998) GAGCTCTCAGTCTCAGCGATCAA (SEQ ID NO:34).

Please replace the paragraph at page 30, lines 1-12, with the following amended paragraph:

## **EXAMPLE 5**

### **EFFECT OF TATA BOX MUTATION ON PROMOTER ACTIVITY**

In order to optimize the function of the promoter its various versions of TATA boxes were tested for promoter activity. Promoter activity was tested experimentally in mice using ELISA to detect anti-hAAT, and luciferase assays. The highest gene expression level was observed when the TATA box sequence TATATAA (SEQ ID NO:30) was the TFIID binding-site whereas, a mutation by deletion of the third T reduced the promoter activity to about 40% as shown in FIG. 2. This result suggests that at least some mutations of the TATA box sequence affecting the TFIID binding-site decreases promoter activity. One of ordinary skill, following the teachings herein will be able to optimize promoter/enhancers using this information.

Please replace the paragraph at page 30, lines 15-25, with the following amended paragraph:

## **EXAMPLE 6**

### **EFFECT OF MULTIPLE TATA BOXES ON PROMOTER ACTIVITY**

In another embodiment of the invention, the effect of multiple TATA boxes on promoter activity was tested. The promoter activity was tested experimentally in mice using ELISA to detect anti-hAAT, and luciferase assays. As demonstrated in FIG. 3, when three TATA boxes (TATATAATATATAATATATAA) (SEQ ID NO:38) are connected instead of a single TATATAA (SEQ ID NO:30) box, the promoter activity is reduced to about 50 %. Thus, the number of TATA boxes proved significant in regulating the promoter activity. This result indicates that, in at least some embodiments of the invention a single TATATAA (SEQ ID NO:30) box is required to achieve the highest promoter activity. One of ordinary skill, following the teachings herein will be able to optimize promoter/enhancers using this information.